**Remarks.**

Entry of the present amendment and reconsideration of the claims is requested. Claims 1, 2, 14, 15, 28, 30 and 34-39 are pending in the instant application. Each amended and new claim has written support in the application; accordingly, no new matter has been added to the application.

Claims 1 and 15 have been amended to replace SEQ ID NO: 4 with SEQ ID NO: 10. Support for this amendment may be found, *e.g.*, in Example 2 of the specification.

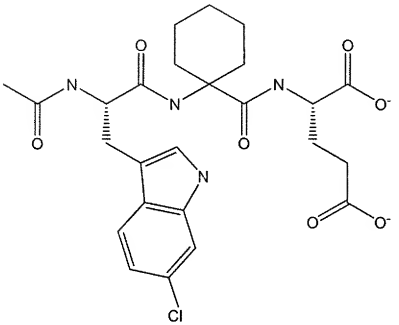
Claims 1, 2 and 15 have been amended to recite a soluble purified polypeptide. Written support for this amendment is, for example, at page 4, lines 11-12.

The remaining amendments make only minor, formal changes which do not add new matter.

New claims 36-39 have been added. Support for these claims may be found, *e.g.*, in the Sequence Listing.

***June 18, 2007 Telephone Interview.*** The applicants thank Examiner's Steadman and Kerr-Bragdon for conducing a telephone interview with the undersigned. During the interview, the written description rejection was discussed. The undersigned contended that the rejection was at odds with, for example, the USPTO Written Description Guidelines and the Trilateral Agreement. The Examiner's contended that the Guidelines and the Agreement did not apply to the instant claims because of differences in the factual circumstances associated with the instant case and because the Guidelines and the Agreement were not hard-and-fast rules, but, instead, were only general guidelines for examination.

*Specification Objections.* The Examiner objected to the specification because it referred to the compound SCH549128 wherein the structure of the compound was unclear. The specification has been amended to delete the term "SCH549128" and insert, in its place, "Ac-6$^{Cl}$WAC$_{3c}$E". This change does not add new matter. The fact that SCH549128 refers to the compound Ac-6$^{Cl}$WAC$_{3c}$E:




is evident for two reasons. First, the description in Example 2 and Table 3 make it clear that the polypeptide is complexed with Ac-6$^{Cl}$WAC$_{3c}$E and that this compound is the same as SCH549128. The coordinates in Table 3 describe the three-dimensional structure of a complex between the polypeptide and Ac-6$^{Cl}$WAC$_{3c}$E. Analysis of the portion of Table 3 describing SCH549128 (*i.e.*, atoms marked "SCH" in the table) would reveal its structure. The atoms describing SCH549128 appear at the end of Table 3. Any practitioner of ordinary skill in the art would appreciate this point. Following Example 3, wherein the polypeptide complex with Ac-6$^{Cl}$WAC$_{3c}$E (SCH549128) was made, the following is stated in the specification just before the Table 3 coordinates:

> The structural coordinates for the above-described Hdm2 crystal are set forth below in Table 3, which is in Protein Data Bank (PDB) file format.

The compound whose structure is described in Table 3 is the same as the compound complexed with the polypeptide in Example 2. Furthermore, Example 2 states that the molecular weight (MW) of SCH549128 is 535. The molecular weight of Ac-6$^{Cl}$WAC$_3$cE (when H saturated) is also 535. Accordingly, the structure of the compound identified by the term SCH549128 is clear. Applicants request withdrawal of this objection.

***Claim Objections.*** The Examiner objects to claims 1, 14 and 28, contending that the oxygens of the carboxy groups of the claimed or recited compounds do not have proper valency. In response, Applicants have amended claims 1, 14 and 28 such that the oxygens of the carboxy groups of the claimed compounds exhibit a negative charge. The Applicants request withdrawal of the objection.

***Claim Rejections under 35 U.S.C. § 112, Second Paragraph.*** Claims 28 and 30 stand rejected as allegedly being indefinite for reciting a formula for compound Ac-$^{6Cl}$WAC$_3$cE that is different from the formula for compound Ac-$^{6Cl}$WAC$_3$cE as identified in the specification. Applicants have amended claims 28 and 30 to recite a formula for compound Ac-$^{6Cl}$WAC$_3$cE that is identical to the formula recited in the specification. Withdrawal of the rejection is appropriate and is requested.

***Rejections under 35 U.S.C. § 112, First Paragraph – Written Description/New Matter/Enablement.*** Claims 1, 2 and 15 stand rejected for alleged lack of adequate written description. The Examiner acknowledges that the specification provides written support for an HDM2 (F55Y/Y76H) polypeptide complex that is soluble at 34 mg/ml concentration, but contends that

"there is no express, implicit, or inherent support for this limitation applying to all of the recited proteins in claims 1 and 15." Office Action, p. 5. Without conceding the correctness of this rejection, Applicants have amended claims 1 and 15 to recite only SEQ ID NO: 10, which is the HDM2 (F55Y/Y76H) polypeptide. Applicants also amended claim 2 to delete the solubility language. Withdrawal of the rejection is requested.

Claims 28 and 30 (and claims 34 and 35 depending therefrom) also stand rejected for an alleged lack of written description. The Examiner states that claims 28 and 30 recite a structural formula for compound Ac-$^{6Cl}$WAC$_3$cE that is different from the structural formula for compound Ac-$^{6Cl}$WAC$_3$cE as identified in the specification. As discussed above in "Claim Rejections under 35 U.S.C. § 112, Second Paragraph," Applicants have amended claims 28 and 30 to recite a formula for compound Ac-$^{6Cl}$WAC$_3$cE that is identical to the formula recited in the specification. Withdrawal of this rejection is appropriate and is requested.

Claims 1, 2 and 15 stand rejected for an alleged lack of written description and enablement. The Examiner contends that these claims may be interpreted as encompassing crystalline polypeptides and complexes thereof, and argues that the specification only discloses and enables a single representative species of the genus of claimed crystals. Without conceding the correctness of this rejection, Applicants have amended claims 1, 2 and 15 to recite a soluble purified polypeptide. Withdrawal of this rejection is appropriate and is requested.

Claims 28, 30, 34 and 35 stand rejected for alleged lack of enablement. The Examiner contends that the expression "having the amino acid sequence" in claims 28 and 30 (and claims 34 and 35 depending therefrom) may been interpreted as being inclusive and open-ended. The Examiner concludes

that these claims thus encompass "crystals of SEQ ID NO:10 or 6 comprising any additional amino acid sequence at the N- and/or C-termini." Office Action, p. 14. Without conceding the correctness of this rejection, Applicants have amended claims 28 and 30 to replace "having the amino acid sequence" with "consisting of the amino acid sequence". Withdrawal of this rejection is appropriate and is requested

The Examiner contends that the specification lacks disclosure that would enable the skilled artisan to make the crystal of SEQ ID NO: 10 or SEQ ID NO: 6. Specifically, the Examiner points out that the specification teaches co-crystallization of the polypeptide of SEQ ID NO:10 with SCH549128, but argues that the structure of SCH549128 is not disclosed in the specification. Further, the Examiner notes that the crystal of claim 28 is a crystal of SEQ ID NO: 10 and Ac-$^{6Cl}$WAC$_3$cE, but contends that the specification does not disclose a method for making such a crystal. Applicants direct the Examiner's attention to the "Specification Objections" section above, which demonstrates that SCH549128 refers to the compound Ac-$^{6Cl}$WAC$_3$cE. Furthermore, Examples 1 and 2 clearly explain how to generate the claimed crystals. Accordingly, the specification enables the skilled worker to make the crystal of SEQ ID NO: 10 and SCH549128 (Ac-$^{6Cl}$WAC$_3$cE).

Finally, the Examiner contends that the specification fails to disclose the concentration of Ac-$^{6Cl}$WAC$_3$cE used in the co-crystallization of Ac-$^{6Cl}$WAC$_3$cE and the polypeptide of SEQ ID NO: 6. As described above, the specification teaches a method for making a crystal of SEQ ID NO: 10 and Ac-$^{6Cl}$WAC$_3$cE (also referred to as SCH549128), wherein the concentration of Ac-$^{6Cl}$WAC$_3$cE is specified as 8.5 mM. One skilled in the art would recognize that the concentration of Ac-$^{6Cl}$WAC$_3$cE used in the co-crystallization of SEQ ID NO: 6, a

similar HDM2 protein, would likely be similar. In any event, even if the concentration of the ligand was not 8.5 mM, modulation of but a single component of the crystallization conditions would not constitute an undue amount of experimentation especially in view of the fact that every other part of the crystallization conditions are explicitly spelled out in Example 3. Applicants request reconsideration and withdrawal of this rejection.

**Conclusion.**

The claims are in condition for allowance. Such action is requested. If the undersigned can be of assistance in advancing the application to allowance, please contact the undersigned at the number set forth below.

Respectfully submitted,

Date: Sept. 6, 2007

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